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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/554,036

10/20/2005

Yevgeni Besidski

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ASTRA ZENECA PHARMACEUTICALS LP
GLOBAL INTELLECTUAL PROPERTY
1800 CONCORD PIKE
WILMINGTON, DE 19850-5437

EXAMINER

STOCKTON, LAURA LYNNE

ART UNIT

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1626

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12/16/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/554,036	Applicant(s) BESIDSKI ET AL.	
	Examiner Laura L. Stockton	Art Unit 1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 25 August 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 21-40 is/are pending in the application.
- 4a) Of the above claim(s) 22,23,26,27,29,30,35-37 and 40 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 21,24,25,28,31-34 and 39 is/are rejected.
- 7) ☒ Claim(s) 38 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>See Continuation Sheet</u> . | 6) <input type="checkbox"/> Other: _____ |

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :March 17, 2006 and March 14, 2008.

DETAILED ACTION

Claims 21-40 are pending in the application.

Election/Restrictions

Applicant's election of Group II (drawn to products of formula I wherein X is S - claims 21, 24, 25, 28, 31-34, 38 and 39) in the reply filed on August 25, 2008 is acknowledged. Compounds not embraced by formula (I) are grouped in new Group VII. See, for instance, some of the compounds in instant claim 38.

Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

The requirement is still deemed proper and is therefore made FINAL.

Subject matter not embraced by elected Group II and Claims 22, 23, 26, 27, 29, 30, 35-37 and 40 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on August 25, 2008.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

The disclosures in the Swedish applications were reviewed because of the possibility of intervening art. The disclosure of the invention in a foreign application in which priority is sought under 35 USC 119(a-d) must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112.

The disclosures of the Swedish applications fail to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. See, for example, the definition of R^3 in Sweden 0301246-5 filed April 28, 2003, the definition of R^3 in Sweden 0301305-9 filed May 5, 2003 and the definitions of R^5 , R^7 and R^8 in Sweden 0400044-4 filed January 12, 2004. Therefore, the instant claimed invention cannot rely on the filing date of any of the Swedish applications but can only rely on the 371 date, which is April 26, 2004.

Information Disclosure Statement

The Examiner has considered the Information Disclosure Statements filed on March 17, 2006 and March 14, 2008.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 21, 24, 25, 28 and 31-33 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

No support in the specification or the originally filed claims can be found for R^3 representing C_1 - $_6$ haloalkyl or hydroxy C_1 - $_6$ alkyl when X is N and R^4 is other than hydrogen. Applicant did not state where {page number(s) and line number(s)} support could be found. Applicant should specifically point out the

support for any amendments. See M.P.E.P. §§ 714.02 and 2163.06.

Claims 21, 24, 25, 28, 31-34 and 39 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a salt of a compound of formula I, does not reasonably provide enablement for a solvate of a compound of formula I or a solvated salt of a compound of formula I. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in making an enablement rejection are summarized as:

- a) the quantity of experimentation necessary,
- b) the amount of direction or guidance presented,
- c) the presence or absence of working examples,
- d) the nature of the invention,

- e) the state of the prior art,
- f) the relative skill of those in the art,
- g) the predictability or unpredictability of the art, and
- h) the breadth of the claims.

In re Colianni, 195 USPQ 150 (CCPA 1977). In re Rainer, et al., 146 USPQ 218 (CCPA 1965). Ex parte Formal, 230 USPQ 546 (BPAI 1986).

a) Determining if a particular compound would form a solvate would require synthesis and recrystallization of the compound solvate using a variety of solvents, temperatures and humidities. The experimentation for solvates is potentially open-ended.

b) The specification merely mentions the Applicant's intention to make solvates, without teaching the preparation thereof.

c) While the claims recite solvates, no working examples show their formation. As stated in Morton

International Inc. v. Cardinal Chemical Co., 28 USPQ2d

1190, 1194 (Fed.Cir. 1993):

The specification purports to teach, with over fifty examples, the preparation of the claimed compounds ... However ... there is no evidence that such compounds exist ... [T]he examples ... do not produce the postulated compounds ... [T]here is ... no evidence that such compounds even exist.

The specification shows no evidence of the formation and actual existence of solvates. Hence, Applicant must show formation of solvates or limit the claims accordingly.

d) The nature of the invention is chemical synthesis of solvates, which involves chemical reactions.

e) The state of the art recognizes that the formation, composition and therapeutic activity of solvates are unpredictable. The Federal Circuit has recognized a solvate as an example of a polymorph or pseudopolymorph (emphasis added):

"Polymorphs" are distinct crystalline structures containing the same molecules. These structural differences can affect various properties of the crystals, such as melting points and hardness (e.g., graphite and diamonds are both crystalline forms of carbon) [P]seudopolymorphs are often loosely called polymorphs ... Pseudopolymorphs not only have their molecules arranged differently but also have a slightly different molecular composition. A common type of pseudopolymorph is a solvate, which is a crystal in which the molecules defining the crystal structure "trap" molecules of a solvent. The crystal molecules and the solvent molecules then bond to form an altered crystalline structure.

SmithKline Beecham Corp. v. Apotex Corp., 74 USPQ2d

1398, 1409 (Fed.Cir. 2005). The same rationale obtains for hydrates; solvates in which the solvent is water.

Souillac, et al., Characterization of Delivery Systems, Differential Scanning Calorimetry, pages 217-218 (in Encyclopedia of Controlled Drug Delivery, 1999, John Wiley & Sons, pages 212-227), recognize that different polymorphs of the same drug can have different therapeutic activity (emphasis added):

Because different polymorphic forms of the same drug exhibit significant differences in their physical characteristics, therapeutic activity

from one form to another may be different.
Studying the polymorphism of a drug and the relative stability of the different polymorphs is a critical part of pre-formulation development.

Further, Vipagunta et al. (Advanced Drug Delivery Reviews, 48 (2001), pages 3-26) state "Predicting the formation of solvates or hydrates of a compound and the number of molecules of water or solvent incorporated in to the crystal lattice of a compound is complex and difficult." See page 18, section 3.4.

f) The artisan using Applicant's disclosure to prepare the claimed solvates would be, e.g., an experienced process chemist with at least a BS chemistry degree.

g) Chemical reactions are known as unpredictable.
In re Marzocchi, et al., 169 USPQ 367, 370 (CCPA 1971);
In re Fisher, 166 USPQ 18, 24 (CCPA 1970). See above regarding the unpredictability of solvate formation.

h) The breadth of the claims includes thousands of compounds of the instant formula I as well as presently

unknown compounds embraced by the terms solvates. See MPEP 2164.01(a), discussed supra, justifying the conclusion of lack of enablement commensurate with the claims. Undue experimentation will be required to practice Applicant's claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 21, 24, 25, 28 and 31-34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 21, line 1 of claim, "having the formula I" should be changed to "of formula I". See claim 34, line 2, for same.

In claim 21, under the definition of ring P, an "or" should be added after "C₃₋₇cycloalkyl", first occurrence. See claim 34 for same.

In claim 21, under the definition of R¹, there is a valence problem in the substituent "C₁₋₆alkylNC₀₋₆alkyl". See claims 31 and 34 for same.

In claim 21, under the definition of R⁴, the proviso at the end of the definition of R⁴ makes claim 21 indefinite because the proviso "is absent when X is N" raises a valence problem when X represents a chalcogen {i.e., O or S} or, since the proviso stipulates that R⁴ is absent when X is N, when X represents N. See claim 25 for same.

In claim 21, under the definition of R⁷ and R⁸, the "and" before "COR⁹" should be deleted and an "and" should be added after "COR⁹". See claim 34 for same.

Claim 24 lacks antecedent basis from claim 21 because the R⁴ is absent in claim 24 but X does not represent N.

In claim 25, under the definition of ring P, an "or" is needed before "C₅₋₆heteroaryl".

In claim 25, next to the last line of claim, an "or" should be added after "phenyl".

Claim 32 lacks antecedent basis from claim 21 when ring P represents pyrazolyl, furan, etc. Note, in claim 21, ring P represents a C₅₋₆heteroaryl whereas pyrazolyl, for instance, has only 3 carbons.

Claim 33 lacks antecedent basis from claim 21 because there are species which are not embraced by claim 21. See, for instance, the 6th, 7th, 9th, etc. species listed in claim 33.

In claim 34, R⁴ being present when X is a chalcogen {i.e., S} raises a valence problem in formula I.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise

extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 21, 24, 25, 31-34 and 39 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-17 and 20 of copending Application No. 11/576,824.

Although the conflicting claims are not identical, they

are not patentably distinct from each other because the instant claimed compounds are generically claimed in the copending application.

The indiscriminate selection of "some" among "many" is *prima facie* obvious, In re Lemin, 141 USPQ 814 (C.C.P.A. 1964). The motivation to make the claimed compounds derives from the expectation that structurally similar compounds would possess similar activity (e.g., treating pain).

One skilled in the art would thus be motivated to prepare products embraced by the copending application to arrive at the instant claimed products with the expectation of obtaining additional beneficial products which would be useful in treating pain. The instant claimed invention would have been suggested to one skilled in the art and therefore, the instant claimed invention would have been obvious to one skilled in the art.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 21, 24, 25 and 31 are rejected under 35 U.S.C. 102(a) as being anticipated by CA Registry No.

519017-23-3, indexed in the Registry file on STN May 22, 2003.

The compound of CA Registry No. 519017-23-3 is embraced by the instant claimed invention. Therefore, CA Registry No. 519017-23-3 anticipates the instant claimed invention.

Claims 21, 24, 25, 28, 31 and 32 are rejected under 35 U.S.C. 102(b) as being anticipated by:

- a) Miller et al. {U.S. Pat. 4,659,738} - see Compound WR 78557 in column 16;
- b) CA Registry No. 477554-53-3 {indexed in the Registry file on STN December 23, 2002};
- c) CA Registry No. 477492-97-0 {indexed in the Registry file on STN December 22, 2002}; or
- d) CA Registry No. 330189-19-0 {indexed in the Registry file on STN April 5, 2001}.

Each of the above cited prior art disclose at least one compound that is embraced by the instant claimed

invention. Therefore, each of the above cited prior art anticipate the instant claimed invention.

Claims 21, 24, 25, 28, 31, 33, 34 and 39 are rejected under 35 U.S.C. 102(e) as being anticipated by Vicker et al. {U.S. Pat. 7,230,020}.

Vicker et al. disclose, for instance, Example 471 in columns 35-36, Example 520 in columns 41-42, etc., which are embraced by the instant claimed invention. Also see columns 20-21 and 134-135. Therefore, Vicker et al. anticipate the instant claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 21, 24, 25, 28, 31, 33, 34 and 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vicker et al. {U.S. Pat. 7,230,020}.

Determination of the scope and content of the prior art (MPEP §2141.01)

Applicant claims benzothiazole compounds. Vicker et al. (see entire document; particularly columns 4-6, 9-15, 20, 21, 134 and 135; and especially Example 471 in columns 35-36) teach benzothiazole compounds that are either structurally the same as (see above 102 rejection) or structurally similar to the instant claimed compounds.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between some of the compounds of Vicker et al. and the compounds instantly claimed is that the instant claimed compounds are generically described in the prior art.

***Finding of prima facie obviousness--rational and motivation (MPEP
§2142-2413)***

The indiscriminate selection of "some" among "many" is *prima facie* obvious, In re Lemin, 141 USPQ 814 (C.C.P.A. 1964). The motivation to make the claimed compounds derives from the expectation that structurally similar compounds would possess similar activity (e.g., an 11 β hydroxysteroid dehydrogenase).

One skilled in the art would thus be motivated to prepare products embraced by the prior art to arrive at the instant claimed products with the expectation of obtaining additional beneficial products which would be useful in treating, for example, hepatic insulin resistance. The instant claimed invention would have been suggested to one skilled in the art and therefore, the instant claimed invention would have been obvious to one skilled in the art.

Allowable Subject Matter

Claim 38 is objected to for containing nonelected subject matter. Claim 38 presented directed solely towards products of formula I wherein X is S (i.e., the elected invention of Group II) would appear allowable over the art of record.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Laura L. Stockton whose telephone number is (571) 272-0710. The examiner can normally be reached on Monday-Friday from 6:00 am to 2:30 pm. If the examiner is out of the Office, the examiner's supervisor, Joseph McKane, can be reached on (571) 272-0699.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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The Official fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

/Laura L. Stockton/
Laura L. Stockton
Primary Examiner, Art Unit 1626
Work Group 1620
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December 16, 2008